

PHA-00373.US1
Serial No.: 10/658,164
Preliminary Amendment

Amendments to Specification

Please replace the paragraph with this typographical inclusion with the paragraph beginning on page 5, line 10 and spanning to page 6, line 2 with the amended paragraph provided herein:

5 The term "dissolution rate" is the rate with which the analyte dissolves in the [[non-]]
aqueous dissolution medium. If the amount of analyte in the aqueous dissolution medium is
determined at only one predetermined time, the dissolution rate is the total amount of analyte,
which has been dissolved up to that predetermined time (e.g. expressed in weight) divided by
10 the predetermined time. For example, if it is determined that 3 μg of analyte have been
dissolved after 30 minutes, the dissolution rate would be 3 $\mu\text{g}/30$ minutes, or 0.1 $\mu\text{g}/\text{minute}$.
If the amount of analyte in the aqueous dissolution medium is determined more than one
time, then the dissolution rate can be illustrated in several different ways, which are known in
the art. One common way is to plot the data in a two-dimensional graph, in which the x-axis
represents the time line and the y-axis represents the amount of analyte dissolved between the
15 nth and the (n-1)th analysis of the aqueous dissolution medium. A further common way is to
plot the data in a two-dimensional graph, in which the x-axis is again a time line and the y-
axis represents the total amount of analyte dissolved between beginning of the measurement
and the nth analysis of the aqueous dissolution medium. Of course the same information can
be presented in a table or any other suitable form other than the two-dimensional graphs
20 discussed above. The following series of experiments can be used as an example: a non-
aqueous liquid composition is investigated and the amount of analyte dissolved is determined
at 10 minutes ($n = 1$), 20 minutes ($n = 2$), and 30 minutes ($n = 3$). After 10 minutes 15 μg of
analyte have dissolved, after 20 minutes 25 μg of analyte have dissolved and after 30 minutes
32 μg of analyte, in total, have dissolved. In the first case the plot as shown in Figure 1 would
25 be obtained, while in the second case the plot would be as in Figure 2.

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Please replace the paragraph with this typographical omission in the paragraph on page 12, lines 19-29 with the amended paragraph provided herein:

5 The amount of the non-aqueous diluent that is added to the non-aqueous liquid
composition is not particularly limiting but is such that it improves the spreading behavior of
the composition non-aqueous liquid. The ratio of the the non-aqueous diluent to the non-
aqueous liquid composition typically ranges from 1: 20 to 20:1, by volume, but can be much
lower or higher. The exact amount may vary depending upon the nature of the analyte, non-
aqueous base, and the dissolution medium. The appropriate amount of the composition and
10 amount of non-aqueous diluent may be determined by one skilled in the art by iterative
empirical evaluations. The relative amount of the composition and diluent may be considered
to be optimal when the diluted composition spreads evenly across the surface of the drug
release medium, or when adequate precision of repeat measurements is obtained.

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Please replace the paragraph beginning on on page 16, line 18, spanning to page 17, line 2 as provided herein:

Aqueous dissolution media employed in the methods of the present invention can be prepared using any type of water such as deionized water, double distilled water or high
5 purity water (i.e. having a resistance of at least about 1 megaohm, more preferably having a resistance of at least about 18 megaohms). Although it is not preferred, tap water can also be used as long as the constituents do not interfere with the measurement. Preferably double distilled water or high purity water, more preferably high purity water, are employed. The use of purer water, especially in combination with a low molarity buffer, has also been observed
10 to increase the precision and reliability of the test results. High purity water can e.g. be provided by using a water purification apparatus such as the Milli-Q water purification systems available from Millipore Corporation (Bedford, Massachusetts). Typically the resultant high purity water has a resistance of about 18 M[[\square]] Ω . The selection of high purity water improves the spreading behavior of the non-aqueous liquid composition upon the
15 surface of the drug release medium, and reduces unwanted interactions between the non-aqueous liquid composition and components of the drug release apparatus (e.g. agitation shaft). By improving the uniformity of spreading and minimizing unwanted physical interactions, it is possible to improve the precision and reliability of the analytical method.